Amendment Under 37 C.F.R. § 1.116 Dated 12/29/04

REMARKS/ARGUMENTS:

Claims 1-31, 33, and 46-54 are cancelled. Claims 37 is withdrawn from consideration. Claim 32 is amended. New claims 55-68 are added. Support for the amendment to claim 32 can be found, e.g., at page 15, lines 22-28 and page 25, line 28 - page 28, line 6 of the specification. Support for new claims 55-68 can be found, e.g., at page 2, line 27 - page 3, line 3; page 3, lines 11-12, 17-21, and 24-30; and page 4, line 1 – page 5, line 16 of the specification. No new matter is introduced. Claims 32, 34-45, and 55-68 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

Claim Rejection Under 35 U.S.C. § 102:

Claims 32, 34-36, and 38-45 are rejected under 35 U.S.C. § 102(a) and (e) as being anticipated by Bennett et al. (U.S. Patent No. 6,066,500; "Bennett"). Applicants respectfully traverses this rejection.

Claim 32, as amended, is directed to a method for inhibiting the expression of a target gene in a substrate that expresses the targeted gene. The method involves two steps: (1) providing a composition comprising an mRNA-cDNA hybrid prior to contacting said substrate, wherein the mRNA-cDNA capable of inhibiting the expression of said targeted gene in said substrate; and (2) contacting said substrate with said composition under conditions such that the expression of said gene in said substrate is inhibited.

The Examiner stated in the Office Action at page 3, lines 4-9:

While the antisense (DNA) oligos of Bennett are single stranded, they become double stranded upon hybridization to their mRNA target. At this point, both method steps have been met, because a DNA/RNA hybrid has been provided and contacted with the substrate (i.e. cell). Therefore, despite the fact that the starting precursors are different from those set forth in applicant's arguments, the final result of Bennett teaches all claim limitations.

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Applicants disagree. Bennett cannot anticipate claim 32 because it fails to teach step (1) of claim 32. More specifically, in the method of claim 32, an mRNA-cDNA hybrid (a double-stranded molecule) is provided prior to contacting a substrate. The providing step of claim 32 (step (1)) is independent of the contacting step (step (2)), i.e., formation of the mRNA-cDNA hybrid does not require contact with the substrate. In contrast, in Bennett, an antisense oligonucleotide (a single-stranded molecule) is contacted with a substrate first, and an mRNA-cDNA hybrid forms after the contacting step (see, e.g., column 3, lines 7-36; column 5, lines 16-28; and column 36, lines 9-18 in Bennett). In other words, the providing step of Bennett is dependent upon the contacting step, i.e., the mRNA-cDNA hybrid does not form if the substrate is not contacted. Thus, Bennett does not anticipate the method of claim 32 because it does not teach all of the limitations of claim 32.

Note that the difference in step (1) between the method of claim 32 and the method of Bennett is of significant importance and is not an obvious variation to a skilled person in the art. Compared to the traditional antisense technology (as described in Bennett), the method of claim 32 provides unexpected advantages such as low dose, stability, and long-term effects in inhibiting the expression of a target gene (see, e.g., page 5, lines 18-19 of the specification). Further, as Bennett requires contact with the substrate for the mRNA-cDNA hybrid to form, it teaches away from the method of claim 32 where the mRNA-cDNA hybrid forms before the substrate is even contacted. Thus, Bennett does not render the claimed method obvious to a person skilled in the art in view of Bennett.

In light of the foregoing, Applicants respectfully submit that Bennett does not anticipate or render obvious claim 32 because it fails to teach or suggest each and every claim limitation. Claims 34-36 and 38-45, as well as new claim 55, depend from claim 32 and cannot be anticipated or rendered obvious for at least the same reasons as claim 32. Withdrawal of this rejection is thus respectfully requested.

New Claims 56-68:

New claim 56, an independent claim, is directed to a method for inhibiting the expression of a target gene in a substrate that expresses the targeted gene. The method involves two steps: (1) providing a composition comprising a synthetic mRNA-cDNA hybrid capable of inhibiting the expression of said targeted gene in said substrate; and (2) contacting said substrate with said composition under conditions such that the expression of said gene in said substrate is inhibited.

This claim is not anticipated by Bennett because Bennett does not teach step (1) of the claim. Specifically, step (1) of claim 56 requires providing a <u>synthetic</u> mRNA-cDNA hybrid, e.g., synthesized using the method described at page 4, line 1 – page 5, line 16 of the specification. In contrast, the mRNA-cDNA hybrid described in Bennett is <u>not</u> a synthetic hybrid; it is formed by hybridization between a cDNA strand (which may or may not be a synthetic strand) introduced into a substrate and its complementary mRNA (which is <u>not</u> a synthetic strand) expressed from a gene in the substrate. Thus, Bennett does not anticipate the method of claim 56 because it fails to teach all of the limitations of claim 56.

Claim 56 is not obvious to a skilled person in the art in view of Bennett because Bennett does not suggest at all synthesis of an mRNA-cDNA hybrid. To the contrary, it relies on the formation of an mRNA-cDNA hybrid once a cDNA is introduced into a substrate and a complementary mRNA is expressed from a gene in the substrate. Claim 56 is also non-obvious because the claimed method provides unexpected advantages as discussed above.

In conclusion, new claim 56 is not anticipated or rendered obvious by Bennett because Bennett fails to teach or suggest each and every claim limitation. New claims 57-68 depend from claim 56 and cannot be anticipated or rendered obvious for at least the same reasons as claim 56.

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In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6853 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted, HOGAN & HARTSON L.L.P.

Dated: December 29, 2004

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